



Clinical trial results:

A Multicenter, Randomized, Double-Blind, Triple-Dummy, Placebo-Controlled, Parallel Group, Four-Week Study Assessing the Efficacy of Fluticasone Propionate Aqueous Nasal Spray 200mcg QD versus Montelukast 10mg QD in Adolescent and Adult Subjects with Asthma and Seasonal Allergic Rhinitis Who are Receiving ADVAIR™ DISKUS™ 100/50mcg BID or Placebo BID

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-004867-35 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 16 June 2007 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 25 January 2017 |
| First version publication date | 25 January 2017 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | ADA103578 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | GlaxoSmithKline |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, |
| Public contact | GSK Response Center, GlaxoSmithKline, 1 866-435-7343, |
| Scientific contact | GSK Response Center, GlaxoSmithKline, 1 866-435-7343, |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 28 September 2007 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 June 2007 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study are to show that fluticasone propionate/salmeterol combination product 100/50mcg (FSC) BID (available as ADVAIR DISKUS) is superior to montelukast 10mg (MON) QD (available as Singulair) as monotherapy for asthma, and that MON administered concurrently with FSC adds no additional benefit to FSC alone in improving asthma control in a population of subjects with allergic asthma. A secondary objective is to demonstrate that in the presence of FSC, FPANS 200mcg QD (available as FLONASE) was superior to MON for control of rhinitis symptoms in a population of subjects with allergic asthma.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 07 September 2005 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United States: 1177 |
| Worldwide total number of subjects | 1177 |
| EEA total number of subjects | 0 |

Notes:

Subjects enrolled per age group

| | |
|---|------|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 90 |
| Adults (18-64 years) | 1053 |
| From 65 to 84 years | 34 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

Participants having diagnosed as persistent asthma, for at least three months, who fulfilled eligibility criteria were enrolled for the study. Six hundred sixty (660) subjects were randomly assigned to one of the four double-blind study treatments

Pre-assignment

Screening details:

Study was conducted at 71 investigational centers in United States. Subjects replaced their current short-acting beta 2-agonist with albuterol to be used as needed throughout the study. After screening, subjects entered a 7-14 day run-in period during which they continued use of their pre-study controller therapy

Period 1

| | |
|------------------------------|---------------------------------|
| Period 1 title | Overall period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|---------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | FSC 100/50mcg (BID)+FPANS (200mcg) QD |

Arm description:

Participants received fluticasone propionate/salmeterol (FSC) 100/50microgram (mcg) inhalation powder twice daily (BID) and fluticasone propionate aqueous nasal spray (FPANS) 200mcg once daily (QD) and placebo capsule once daily for four weeks.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Fluticasone propionate/salmeterol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Oral use |

Dosage and administration details:

100/50mcg twice a day

| | |
|--|--|
| Investigational medicinal product name | Fluticasone propionate aqueous nasal spray |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation vapour |
| Routes of administration | Nasal use |

Dosage and administration details:

200mcg once daily

| | |
|------------------|------------------------------------|
| Arm title | FSC 100/50mcg (BID) +MON 10mg (QD) |
|------------------|------------------------------------|

Arm description:

Participants received fluticasone propionate/salmeterol 100/50mcg Inhalation powder twice daily, Montelukast (MON) 10mg capsule once daily and vehicle placebo nasal spray once daily for four weeks.

| | |
|--|-----------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Fluticasone propionate/salmeterol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Oral use |

| | |
|--|-----------------------------------|
| Dosage and administration details: 100/50mcg twice a day | |
| Investigational medicinal product name | Montelukast |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: 10mg once daily | |
| Arm title | FSC 100/50mcg (BID) |
| Arm description: Participants received fluticasone propionate/salmeterol 100/50mcg Inhalation powder twice daily, vehicle placebo nasal spray once daily and placebo capsule once daily for four weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Fluticasone propionate/salmeterol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation powder |
| Routes of administration | Oral use |
| Dosage and administration details: 100/50mcg twice a day | |
| Arm title | MON 10mg (QD) |
| Arm description: Participants received Montelukast 10mg capsule once daily, placebo via dry powder inhaler BID, and vehicle placebo nasal spray QD for four weeks. | |
| Arm type | Active comparator |
| Investigational medicinal product name | Montelukast |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: 10mg once daily | |

| Number of subjects in period 1^[1] | FSC 100/50mcg (BID)+FPANS (200mcg) QD | FSC 100/50mcg (BID) +MON 10mg (QD) | FSC 100/50mcg (BID) |
|---|---------------------------------------|------------------------------------|---------------------|
| Started | 168 | 165 | 157 |
| Completed | 139 | 139 | 125 |
| Not completed | 29 | 26 | 32 |
| Consent withdrawn by subject | - | 1 | - |
| Physician decision | - | - | 1 |
| Adverse event, non-fatal | 5 | 2 | 3 |
| Other; reasons not specified | 7 | 8 | 12 |
| Other; Exacerbation | 1 | 1 | 2 |
| Lost to follow-up | 1 | 2 | - |
| Protocol deviation | 6 | 3 | 3 |

| | | | |
|-----------------------|---|---|----|
| Other; Non-compliance | 9 | 9 | 11 |
| Lack of efficacy | - | - | - |

| Number of subjects in period 1^[1] | MON 10mg (QD) |
|---|---------------|
| Started | 170 |
| Completed | 134 |
| Not completed | 36 |
| Consent withdrawn by subject | 4 |
| Physician decision | - |
| Adverse event, non-fatal | 2 |
| Other; reasons not specified | 13 |
| Other; Exacerbation | 5 |
| Lost to follow-up | - |
| Protocol deviation | 1 |
| Other; Non-compliance | 10 |
| Lack of efficacy | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Although 1177 participants enrolled, a total of 660 subjects comprised the Intent-To-Treat population randomized into the study. Sixty three (63) sites randomized a total of 396 subjects into a Per Protocol population.

Baseline characteristics

Reporting groups

| | |
|--|---------------------------------------|
| Reporting group title | FSC 100/50mcg (BID)+FPANS (200mcg) QD |
| Reporting group description: | |
| Participants received fluticasone propionate/salmeterol (FSC) 100/50microgram (mcg) inhalation powder twice daily (BID) and fluticasone propionate aqueous nasal spray (FPANS) 200mcg once daily (QD) and placebo capsule once daily for four weeks. | |
| Reporting group title | FSC 100/50mcg (BID) +MON 10mg (QD) |
| Reporting group description: | |
| Participants received fluticasone propionate/salmeterol 100/50mcg Inhalation powder twice daily, Montelukast (MON) 10mg capsule once daily and vehicle placebo nasal spray once daily for four weeks. | |
| Reporting group title | FSC 100/50mcg (BID) |
| Reporting group description: | |
| Participants received fluticasone propionate/salmeterol 100/50mcg Inhalation powder twice daily, vehicle placebo nasal spray once daily and placebo capsule once daily for four weeks. | |
| Reporting group title | MON 10mg (QD) |
| Reporting group description: | |
| Participants received Montelukast 10mg capsule once daily, placebo via dry powder inhaler BID, and vehicle placebo nasal spray QD for four weeks. | |

| Reporting group values | FSC 100/50mcg (BID)+FPANS (200mcg) QD | FSC 100/50mcg (BID) +MON 10mg (QD) | FSC 100/50mcg (BID) |
|--|---------------------------------------|------------------------------------|---------------------|
| Number of subjects | 168 | 165 | 157 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 36.2 ± 13.12 | 36.6 ± 12.47 | 37.4 ± 13.85 |
| Gender categorical Units: | | | |
| Female | 116 | 120 | 108 |
| Male | 52 | 45 | 49 |
| Race, Customized | | | |
| Please note: The unknown category is used to present 1 participant who is missing from the study's demographic table in arm: FSC 100/50mcg (BID)+FPANS (200mcg) QD. There is no further explanation provided about the 1 missing participant data. | | | |
| Units: Subjects | | | |
| African American/African Heritage | 18 | 19 | 22 |
| American Indian or Alaska Native | 3 | 3 | 0 |
| Asian - Central/South Asian Heritage | 2 | 3 | 1 |
| Asian - East Asian Heritage | 1 | 2 | 1 |
| Asian - Japanese Heritage | 0 | 2 | 0 |
| Asian - South East Asian Heritage | 1 | 3 | 1 |
| Native Hawaiian or other Pacific Islander | 1 | 1 | 1 |
| White - Arabic/North African Heritage | 2 | 1 | 0 |

| | | | |
|---|-----|-----|-----|
| White - White/Caucasian/European Heritage | 137 | 130 | 129 |
| White - Mixed Race | 1 | 0 | 0 |
| Mixed Race | 1 | 1 | 2 |
| Unknown | 1 | 0 | 0 |

| Reporting group values | MON 10mg (QD) | Total | |
|------------------------|---------------|-------|--|
| Number of subjects | 170 | 660 | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------|--------|-----|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 36.7 | | |
| standard deviation | ± 13.9 | - | |
| Gender categorical | | | |
| Units: | | | |
| Female | 108 | 452 | |
| Male | 62 | 208 | |
| Race, Customized | | | |

Please note: The unknown category is used to present 1 participant who is missing from the study's demographic table in arm: FSC 100/50mcg (BID)+FPANS (200mcg) QD. There is no further explanation provided about the 1 missing participant data.

| | | | |
|---|-----|-----|--|
| Units: Subjects | | | |
| African American/African Heritage | 19 | 78 | |
| American Indian or Alaska Native | 3 | 9 | |
| Asian - Central/South Asian Heritage | 2 | 8 | |
| Asian - East Asian Heritage | 0 | 4 | |
| Asian - Japanese Heritage | 0 | 2 | |
| Asian - South East Asian Heritage | 1 | 6 | |
| Native Hawaiian or other Pacific Islander | 1 | 4 | |
| White - Arabic/North African Heritage | 2 | 5 | |
| White - White/Caucasian/European Heritage | 142 | 538 | |
| White - Mixed Race | 0 | 1 | |
| Mixed Race | 0 | 4 | |
| Unknown | 0 | 1 | |

End points

End points reporting groups

| | |
|--|---------------------------------------|
| Reporting group title | FSC 100/50mcg (BID)+FPANS (200mcg) QD |
| Reporting group description: Participants received fluticasone propionate/salmeterol (FSC) 100/50microgram (mcg) inhalation powder twice daily (BID) and fluticasone propionate aqueous nasal spray (FPANS) 200mcg once daily (QD) and placebo capsule once daily for four weeks. | |
| Reporting group title | FSC 100/50mcg (BID) +MON 10mg (QD) |
| Reporting group description: Participants received fluticasone propionate/salmeterol 100/50mcg Inhalation powder twice daily, Montelukast (MON) 10mg capsule once daily and vehicle placebo nasal spray once daily for four weeks. | |
| Reporting group title | FSC 100/50mcg (BID) |
| Reporting group description: Participants received fluticasone propionate/salmeterol 100/50mcg Inhalation powder twice daily, vehicle placebo nasal spray once daily and placebo capsule once daily for four weeks. | |
| Reporting group title | MON 10mg (QD) |
| Reporting group description: Participants received Montelukast 10mg capsule once daily, placebo via dry powder inhaler BID, and vehicle placebo nasal spray QD for four weeks. | |

Primary: Change from baseline in morning peak expiratory flow to assess superiority

| | |
|--|--|
| End point title | Change from baseline in morning peak expiratory flow to assess superiority |
| End point description: Peak expiratory flow (PEF) was measured by the participant between clinic visits using the device used for spirometry assessments. Change from baseline is calculated as endpoint value minus baseline value where endpoint was defined as the average of the last (week 4) week's worth of data. Superiority analysis was performed by comparing the values between treatment groups. The Intent-to-Treat (ITT) population was defined as all subjects randomized to double-blind treatment | |
| End point type | Primary |
| End point timeframe: Baseline and Week 4 | |

| End point values | FSC 100/50mcg (BID)+FPANS (200mcg) QD | FSC 100/50mcg (BID) +MON 10mg (QD) | FSC 100/50mcg (BID) | MON 10mg (QD) |
|---------------------------------|---------------------------------------|------------------------------------|---------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 165 ^[1] | 161 ^[2] | 154 ^[3] | 162 ^[4] |
| Units: Liter per minute (L/min) | | | | |
| geometric mean (standard error) | 20.8 (± 3.31) | 28.7 (± 3.06) | 28.9 (± 3.99) | -2.2 (± 3.5) |

Notes:

[1] - Intent-to-treat (ITT) population.

[2] - ITT Population

[3] - ITT Population

[4] - ITT Population

Statistical analyses

| | |
|---|-------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | MON 10mg (QD) v FSC 100/50mcg (BID) |
| Number of subjects included in analysis | 316 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | 29.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 20.1 |
| upper limit | 39.4 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.92 |

Primary: Mean change from baseline in morning peak expiratory flow to assess equivalence

| | |
|-----------------|---|
| End point title | Mean change from baseline in morning peak expiratory flow to assess equivalence |
|-----------------|---|

End point description:

PEF was measured by the participant between clinic visits using the device used for spirometry assessments. Change from baseline is calculated as endpoint value minus baseline value where endpoint was defined as the average of the last (week 4) week's worth of data. Equivalence comparison was significant if Confidence interval falls entirely within (-18, 18) and contains zero. Per protocol (PP) population is defined as analysis can only be restricted to the participants who fulfill the protocol in the terms of the eligibility, interventions, and outcome assessment.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and Week 4

| End point values | FSC 100/50mcg (BID)+FPANS (200mcg) QD | FSC 100/50mcg (BID) +MON 10mg (QD) | FSC 100/50mcg (BID) | MON 10mg (QD) |
|---------------------------------|--|---|---------------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 105 ^[5] | 115 ^[6] | 78 ^[7] | 98 ^[8] |
| Units: Liter per minute (L/min) | | | | |
| geometric mean (standard error) | 20.8 (± 3.84) | 32.4 (± 3.66) | 37 (± 6.75) | 1.9 (± 4.61) |

Notes:

[5] - Per protocol population

[6] - Per protocol population

[7] - Per protocol population

[8] - Per protocol population

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | FSC 100/50mcg (BID) +MON 10mg (QD) v FSC 100/50mcg (BID) |
| Number of subjects included in analysis | 193 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence ^[9] |
| P-value | = 0.006 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.4 |
| upper limit | 14.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.02 |

Notes:

[9] - Equivalence comparison is significant if CI falls entirely within (-18, 18) and contains zero.

Secondary: Change from baseline in daytime total nasal symptom scores.

| | |
|---|---|
| End point title | Change from baseline in daytime total nasal symptom scores. |
| End point description: | |
| Nasal symptoms were evaluated by the subject using 4-point (0 to 3) categorical scale, where 0-none, 1-mild, 2-moderate and 3-severe. The scores of the four component daytime symptoms (nasal congestion, itching, rhinorrhea, and sneezing) were summed to create a Daytime Total Nasal Symptom Score (D-TNSS) for each day. Change from baseline was calculated as Weeks 1-2 values minus baseline value, where values between week 1 and week 2 were averaged for Week 1-2 value. Confidence intervals and p-values are corrected for multiplicity using Hochberg's method. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Weeks 1-2 | |

| End point values | FSC 100/50mcg (BID)+FPANS (200mcg) QD | FSC 100/50mcg (BID) +MON 10mg (QD) | FSC 100/50mcg (BID) | MON 10mg (QD) |
|---------------------------------|---------------------------------------|------------------------------------|---------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 167 ^[10] | 162 ^[11] | 155 ^[12] | 167 ^[13] |
| Units: Scores | | | | |
| geometric mean (standard error) | -3.3 (± 0.18) | -2.5 (± 0.16) | -2.3 (± 0.17) | -2.4 (± 0.15) |

Notes:

[10] - ITT Population

[11] - ITT Population

[12] - ITT Population

[13] - ITT Population

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | FSC 100/50mcg (BID)+FPANS (200mcg) QD v FSC 100/50mcg |

| | |
|---|------------------------------|
| | (BID) +MON 10mg (QD) |
| Number of subjects included in analysis | 329 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.4 |
| upper limit | -0.4 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.22 |

Secondary: Change from baseline in night time total nasal symptoms.

| | |
|-----------------|--|
| End point title | Change from baseline in night time total nasal symptoms. ^[14] |
|-----------------|--|

End point description:

Nasal symptoms were evaluated by the subject using 4-point (0 to 3) categorical scale, where 0-none, 1-mild, 2-moderate and 3-severe. The sum of symptom scores assessing AM nasal congestion upon wakening, difficulty in going to sleep due to nasal symptoms, and night time awakenings due to nasal symptoms. Change from baseline was calculated as Weeks 1-2 values minus baseline value, where values between week 1 and week 2 were averaged for Week 1-2 value. Confidence intervals and p-values are corrected for multiplicity using Hochberg's method.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to weeks 1-2

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis is presented as available. Statistical analysis is not available for all the baseline period arms.

| End point values | FSC 100/50mcg (BID)+FPANS (200mcg) QD | FSC 100/50mcg (BID) +MON 10mg (QD) | | |
|---------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 167 ^[15] | 161 ^[16] | | |
| Units: Scores | | | | |
| geometric mean (standard error) | -2.1 (± 0.13) | -1.8 (± 0.12) | | |

Notes:

[15] - ITT Population

[16] - ITT Population

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | FSC 100/50mcg (BID)+FPANS (200mcg) QD v FSC 100/50mcg (BID) +MON 10mg (QD) |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 328 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.005 |
| Method | ANCOVA |
| Parameter estimate | least square mean difference |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.7 |
| upper limit | -0.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.15 |

Secondary: Change from baseline at endpoint in predose AM FEV1

| | |
|---|---|
| End point title | Change from baseline at endpoint in predose AM FEV1 ^[17] |
| End point description: | |
| Forced expiratory volume in one second (FEV1) was evaluated. Change from baseline is calculated as endpoint value minus baseline value where baseline FEV1 was defined as the measure recorded on the morning of Day 1, just prior to randomization and endpoint was defined as the last available on-treatment FEV1 measure. Confidence intervals and p-values are corrected for multiplicity using Hochberg's method. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and week 4 | |

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis is presented as available. Statistical analysis is not available for all the baseline period arms.

| End point values | FSC 100/50mcg (BID) | MON 10mg (QD) | | |
|---------------------------------|---------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 143 ^[18] | 153 ^[19] | | |
| Units: Liter (L) | | | | |
| geometric mean (standard error) | 0.21 (± 0.0277) | 0.057 (± 0.026) | | |

Notes:

[18] - ITT Population

[19] - ITT Population

Statistical analyses

| | |
|----------------------------|-------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | FSC 100/50mcg (BID) v MON 10mg (QD) |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 296 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | 0.131 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.056 |
| upper limit | 0.207 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0335 |

Secondary: Mean change from baseline in predose morning (AM) FEV1 to assess equivalence

| | |
|-----------------|--|
| End point title | Mean change from baseline in predose morning (AM) FEV1 to assess equivalence ^[20] |
|-----------------|--|

End point description:

Forced expiratory volume in one second (FEV1) was evaluated. Change from baseline is calculated as endpoint value minus baseline value where baseline FEV1 was defined as the measure recorded on the morning of Day 1, just prior to randomization and endpoint was defined as the last available on-treatment FEV1 measure. Confidence intervals and p-values are corrected for multiplicity using Hochberg's method

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and week 4

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis is presented as available. Statistical analysis is not available for all the baseline period arms.

| End point values | FSC 100/50mcg (BID) +MON 10mg (QD) | FSC 100/50mcg (BID) | | |
|---------------------------------|---|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 113 ^[21] | 77 ^[22] | | |
| Units: Liter (L) | | | | |
| geometric mean (standard error) | 0.217 (± 0.0253) | 0.219 (± 0.0376) | | |

Notes:

[21] - Per protocol (PP) population

[22] - PP Population

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | FSC 100/50mcg (BID) +MON 10mg (QD) v FSC 100/50mcg (BID) |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 190 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence ^[23] |
| P-value | = 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | 0.053 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.05 |
| upper limit | 0.156 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0429 |

Notes:

[23] - Equivalence comparison is significant if CI falls entirely within (-0.2, 0.2) and contains zero.

Secondary: Change from baseline in the asthma symptom free-days

| | |
|------------------------|---|
| End point title | Change from baseline in the asthma symptom free-days ^[24] |
| End point description: | Subject rated overall satisfaction with treatment was analyzed by Percentage of Asthma Symptom-free Days. Change from baseline is calculated as endpoint value minus baseline value, where, Endpoint is defined as the average of the last seven days' worth of data. Confidence intervals and p-values are corrected for multiplicity using Hochberg's method. |
| End point type | Secondary |
| End point timeframe: | Baseline and week 4 |

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis is presented as available. Statistical analysis is not available for all the baseline period arms.

| End point values | FSC 100/50mcg (BID) | MON 10mg (QD) | | |
|---------------------------------|---------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 ^[25] | 161 ^[26] | | |
| Units: Percentage | | | | |
| geometric mean (standard error) | 32.1 (± 2.99) | 13.9 (± 2.43) | | |

Notes:

[25] - ITT Population

[26] - ITT Population

Statistical analyses

| | |
|----------------------------|-------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | FSC 100/50mcg (BID) v MON 10mg (QD) |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 316 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | 18.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 8.7 |
| upper limit | 28.3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.09 |

Secondary: Change from baseline in asthma symptom-free days

| | |
|------------------------|---|
| End point title | Change from baseline in asthma symptom-free days ^[27] |
| End point description: | Subject rated overall satisfaction with treatment was analyzed by Percentage of Asthma Symptom-free Days. Change from baseline is calculated as endpoint value minus baseline value, where, Endpoint is defined as the average of the last seven days' worth of data. Confidence intervals and p-values are corrected for multiplicity using Hochberg's method. |
| End point type | Secondary |
| End point timeframe: | Baseline and Week 4 |

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis is presented as available. Statistical analysis is not available for all the baseline period arms.

| End point values | FSC 100/50mcg (BID) +MON 10mg (QD) | FSC 100/50mcg (BID) | | |
|---------------------------------|---|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 115 ^[28] | 78 ^[29] | | |
| Units: Percentage | | | | |
| geometric mean (standard error) | 37.3 (± 3.72) | 35.7 (± 4.18) | | |

Notes:

[28] - PP Population

[29] - PP Population

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | Equivalence comparison is significant if CI falls entirely within (-15.7, 15.7) and contains zero. |
| Comparison groups | FSC 100/50mcg (BID) +MON 10mg (QD) v FSC 100/50mcg (BID) |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 193 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.017 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | 3.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.6 |
| upper limit | 14.8 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 5.69 |

Secondary: Change from baseline in the percentage of albuterol-free-days

| | |
|-----------------|---|
| End point title | Change from baseline in the percentage of albuterol-free- |
|-----------------|---|

End point description:

Overall satisfaction with treatment was analyzed by percentage of albuterol-free-days (puffs/24hour [hr]). Change from baseline is calculated as endpoint value minus baseline value, where, Endpoint is defined as the average of the last seven days' worth of data. Confidence intervals and p-values are corrected for multiplicity using Hochberg's method.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Week 4

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis is presented as available. Statistical analysis is not available for all the baseline period arms.

| End point values | FSC 100/50mcg (BID) | MON 10mg (QD) | | |
|---------------------------------|---------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 ^[31] | 161 ^[32] | | |
| Units: Percentage | | | | |
| geometric mean (standard error) | 37 (± 3.18) | 21.4 (± 2.83) | | |

Notes:

[31] - ITT Population

[32] - ITT Population

Statistical analyses

| | |
|----------------------------|-------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | FSC 100/50mcg (BID) v MON 10mg (QD) |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 316 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | 15.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7.5 |
| upper limit | 24.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.22 |

Secondary: Change from baseline in percentage of Albuterol-free days .

| | |
|---|---|
| End point title | Change from baseline in percentage of Albuterol-free days . ^[33] |
| End point description: | |
| Overall satisfaction with treatment was analyzed by Percentage of albuterol-free-days (puffs/24hr). Change from baseline is calculated as endpoint value minus baseline value, where, Endpoint is defined as the average of the last seven days' worth of data. Confidence intervals and p-values are corrected for multiplicity using Hochberg's method. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 4 | |

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis is presented as available. Statistical analysis is not available for all the baseline period arms.

| End point values | FSC 100/50mcg (BID) +MON 10mg (QD) | FSC 100/50mcg (BID) | | |
|---------------------------------|---|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 115 ^[34] | 78 ^[35] | | |
| Units: Percentage | | | | |
| geometric mean (standard error) | 39.1 (± 3.73) | 43.4 (± 4.54) | | |

Notes:

[34] - PP Population

[35] - PP Population

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | FSC 100/50mcg (BID) +MON 10mg (QD) v FSC 100/50mcg (BID) |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 193 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence ^[36] |
| P-value | = 0.007 |
| Method | ANCOVA |
| Parameter estimate | least square mean difference |
| Point estimate | -3.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.8 |
| upper limit | 10 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 5.95 |

Notes:

[36] - Equivalence comparison is significant if CI falls entirely within (-19.5, 19.5) and contains zero.

Secondary: Subject Rated Overall Satisfaction with Treatment.

| | |
|--|--|
| End point title | Subject Rated Overall Satisfaction with Treatment. |
| End point description: | |
| Subject-rated overall satisfaction with treatment (related to percentage of asthma symptom-free days). The satisfaction category ranged from very dissatisfied to very satisfied. The measurement type refers to the number of participants. | |
| End point type | Secondary |
| End point timeframe: | |
| At Week 4 | |

| End point values | FSC 100/50mcg (BID)+FPANS (200mcg) QD | FSC 100/50mcg (BID) +MON 10mg (QD) | FSC 100/50mcg (BID) | MON 10mg (QD) |
|-----------------------------|--|---|---------------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 95 | 106 | 71 | 96 |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Very dissatisfied | 0 | 0 | 1 | 6 |
| Dissatisfied | 3 | 4 | 3 | 14 |
| Slightly dissatisfied | 11 | 7 | 12 | 9 |
| Neutral | 12 | 15 | 8 | 16 |
| Slight satisfied | 14 | 19 | 16 | 11 |
| Satisfied | 29 | 39 | 22 | 33 |
| Very satisfied | 26 | 22 | 9 | 7 |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in evening (PM) peak expiratory flow.

| | |
|-----------------|--|
| End point title | Change from baseline in evening (PM) peak expiratory flow. ^[37] |
|-----------------|--|

End point description:

Evening peak expiratory flow (PM PEF) was measured using the device used for spirometry assessments. Change from baseline is calculated as endpoint value minus baseline value where endpoint was defined as the average of the last (week 4) week's worth of data. Superiority analysis was performed by comparing the values between treatment groups.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Week 4

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis is presented as available. Statistical analysis is not available for all the baseline period arms.

| End point values | FSC 100/50mcg (BID) | MON 10mg (QD) | | |
|---------------------------------|---------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 ^[38] | 161 ^[39] | | |
| Units: Liter per minutes | | | | |
| geometric mean (standard error) | 18.3 (± 3.91) | -9.7 (± 3.38) | | |

Notes:

[38] - ITT Population

[39] - ITT Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|-------------------------------------|
| Comparison groups | FSC 100/50mcg (BID) v MON 10mg (QD) |
| Number of subjects included in analysis | 316 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | 25.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 16.2 |
| upper limit | 35.3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.85 |

Secondary: Change from Baseline in Asthma Symptom Scores.

| | |
|-----------------|--|
| End point title | Change from Baseline in Asthma Symptom Scores. ^[40] |
|-----------------|--|

End point description:

Asthma symptom scores are diary-based asthma measures related to the proportion of asthma symptom-free days. Change from baseline is calculated as endpoint value minus baseline value where

endpoint was defined as the average of the last (week 4) week's worth of data. Superiority analysis was performed by comparing the values between treatment groups.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Week 4

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis is presented as available. Statistical analysis is not available for all the baseline period arms.

| End point values | FSC 100/50mcg (BID) | MON 10mg (QD) | | |
|---------------------------------|---------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 157 ^[41] | 170 ^[42] | | |
| Units: Scores | | | | |
| geometric mean (standard error) | -1.3 (\pm 0.07) | -1 (\pm 0.09) | | |

Notes:

[41] - ITT Population

[42] - ITT Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|-------------------------------------|
| Comparison groups | FSC 100/50mcg (BID) v MON 10mg (QD) |
| Number of subjects included in analysis | 327 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | -0.346 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.539 |
| upper limit | -0.152 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.0985 |

Secondary: Mean Change from Baseline in daily albuterol use.

| | |
|-----------------|---|
| End point title | Mean Change from Baseline in daily albuterol use. ^[43] |
|-----------------|---|

End point description:

Daily albuterol use (puffs/24hr) is a diary-based asthma measures. Change from baseline is calculated as endpoint value minus baseline value where endpoint was defined as the average of the last (week 4) week's worth of data. Superiority analysis was performed by comparing the values between treatment groups.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to endpoint

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis is presented as available. Statistical analysis is not available for all the baseline period arms.

| End point values | FSC 100/50mcg (BID) | MON 10mg (QD) | | |
|---------------------------------|---------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 ^[44] | 161 ^[45] | | |
| Units: Puffs per 24 hours | | | | |
| geometric mean (standard error) | -1.5 (± 0.14) | -1 (± 0.15) | | |

Notes:

[44] - ITT Population

[45] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Daytime Nasal Congestion Symptom Score.

| | |
|-----------------|--|
| End point title | Mean Change from Baseline in Daytime Nasal Congestion Symptom Score. ^[46] |
|-----------------|--|

End point description:

Nasal congestion symptom score were evaluated by the subject using 4-point (0 to 3) categorical scale, where 0-none, 1-mild, 2-moderate and 3-severe. Change from baseline is calculated as treatment Week 1-2 value minus baseline value where Week 1-2 was defined as the average of data recorded from Day 2 to Day 15. Superiority analysis was performed by comparing the values between treatment groups.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Weeks 1-2

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis is presented as available. Statistical analysis is not available for all the baseline period arms.

| End point values | FSC 100/50mcg (BID)+FPANS (200mcg) QD | FSC 100/50mcg (BID) +MON 10mg (QD) | | |
|---------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 168 ^[47] | 165 ^[48] | | |
| Units: Score on scale | | | | |
| geometric mean (standard error) | -0.8 (± 0.05) | -0.6 (± 0.04) | | |

Notes:

[47] - ITT Population

[48] - ITT Population

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | FSC 100/50mcg (BID)+FPANS (200mcg) QD v FSC 100/50mcg (BID) +MON 10mg (QD) |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 333 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.3 |
| upper limit | -0.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.06 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse event (SAE) and non serious adverse event (non-SAE) was analyzed up to 4 week of the study.

Adverse event reporting additional description:

All AE were based on the ITT population. AEs were sorted by system organ class (SOC).

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 10.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------------------|
| Reporting group title | FSC 100/50mcg (BID)+FPANS (200mcg) QD |
|-----------------------|---------------------------------------|

Reporting group description:

Participants received fluticasone propionate/salmeterol (FSC) 100/50microgram (mcg) Inhalation powder twice daily (BID) and fluticasone propionate aqueous nasal spray (FPANS) 200mcg once daily (QD) and placebo capsule once daily for four weeks.

| | |
|-----------------------|------------------------------------|
| Reporting group title | FSC 100/50mcg (BID) +MON 10mg (QD) |
|-----------------------|------------------------------------|

Reporting group description:

Participants received fluticasone propionate/salmeterol 100/50mcg Inhalation powder twice daily, Montelukast (MON) 10mg capsule once daily and vehicle placebo nasal spray once daily for four weeks.

| | |
|-----------------------|---------------------|
| Reporting group title | FSC 100/50mcg (BID) |
|-----------------------|---------------------|

Reporting group description:

Participants received fluticasone propionate/salmeterol 100/50mcg Inhalation powder twice daily, vehicle placebo nasal spray once daily and placebo capsule once daily for four weeks.

| | |
|-----------------------|---------------|
| Reporting group title | MON 10mg (QD) |
|-----------------------|---------------|

Reporting group description:

Participants received Montelukast 10mg capsule once daily, placebo via dry powder inhaler BID, and vehicle placebo nasal spray QD for four weeks.

| Serious adverse events | FSC 100/50mcg (BID)+FPANS (200mcg) QD | FSC 100/50mcg (BID) +MON 10mg (QD) | FSC 100/50mcg (BID) |
|---|---------------------------------------|------------------------------------|---------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 165 (0.00%) | 0 / 157 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 168 (0.00%) | 0 / 165 (0.00%) | 0 / 157 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | MON 10mg (QD) | | |
|------------------------------------|---------------|--|--|
| Total subjects affected by serious | | | |

| | | | |
|---|-----------------|--|--|
| adverse events | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Pelvic fracture | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 3 %

| Non-serious adverse events | FSC 100/50mcg (BID)+FPANS (200mcg) QD | FSC 100/50mcg (BID) +MON 10mg (QD) | FSC 100/50mcg (BID) |
|---|---------------------------------------|------------------------------------|---------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 13 / 168 (7.74%) | 8 / 165 (4.85%) | 7 / 157 (4.46%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 13 / 168 (7.74%) | 8 / 165 (4.85%) | 7 / 157 (4.46%) |
| occurrences (all) | 15 | 8 | 7 |

| Non-serious adverse events | MON 10mg (QD) | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 17 / 170 (10.00%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 17 / 170 (10.00%) | | |
| occurrences (all) | 34 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 28 July 2005 | Replaced all instances of Ventolin Hydrofluoroalkane (HFA) with albuterol/salbutamol. Clarified selection method for best spirometry effort. Included complete rating scale for patient satisfaction with treatment questionnaire. |
| 17 October 2006 | Amended Sponsor Contact Information Page. Clarified Statistical Analyses sections. |
| 12 January 2007 | Increased number of randomized subjects, revised participating countries, expanded acceptable visit windows, and corrected administrative errors |
| 14 May 2007 | Amended Sponsor Contact Information Page, revised asthma therapy footnote to include ADVAIR HFA and Symbicort, and included ciclesonide as allowable prior asthma therapy |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported